REMARKS

Claims 1-3, 5, 10, 11, 13 and 18-21 are pending. Claims 4, 15 and 16 have been cancelled without prejudice. Claims 1-3, 5, 10 and 11 have been amended. However, the cancellation of and/or amendments to the claims have been made solely to expedite prosecution of the present application. New claims 18-21 have been added. Support for the new claims can be found throughout the present application. No new matter has been added.

Rejection of Claims 15 and 16 Under 35 U.S.C. §112, first paragraph

Claims 15 and 16 are rejected under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention."

Claims 15 and 16 have been cancelled, thereby obviating this rejection.

Rejection of Claims 1, 3-5, 10, 11, 13 and 15 Under 35 U.S.C. §112, first paragraph

Claims 1, 3-5, 10, 11, 13 and 15 are rejected under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." According to the Examiner,

> [t]he invention comprises the genuses of Helios gene and fragments thereof. These genuses would appear to include sequences which encode functional Helios proteins. They may include fragments of Helios, and other variants comprising deletions, substitutions, insertions, additions, or replacements of the Helios sequences. Since there is no language describing functional limitations of the claimed sequences the claimed nucleic acid sequences also include sequences which do not encode a functional Helios protein. The genus also conventionally includes genomic clones of genes encoding these polypeptides, comprising introns and natural promoters since there would also hybridize to SEQ ID NO: 1, 3 or 5.

Claims 4 and 15 have been cancelled without prejudice, thereby obviating this rejection with regard to those claims. Independent claims 1 and 3 (from which claims 10, 11 and 13 directly or indirectly depend) have been amended such that the claimed nucleic acids not only have structural limitations, namely at least 80% identity or ability to hybridize under high stringency conditions to listed sequences, but also are functionally limited to those sequences which also encode a polypeptide having a Helios biological activity. Helios biological activities are provided throughout the present application. See, e.g., page 33, lines16-21.

The Examiner states that

> [n]o correlation has been disclosed between any 60% identical sequence and any protein structure which is sufficient for biological activity. The specification only describes sequences which have an appropriate biological function of Helios as a transcription factor, which functions in concert with other polypeptides which are part of the Ikaros gene family. The specification does not describe sequences which have this biological function for any sequence 60% identical to SEQ ID NO: 1, 3, or 5. Because the specification fails to describe more than a single species of each genus, and because one of skill in the art could not be expected to predict the biological activity of the sequence variants encompassed by the claims, the written description requirement has not been met.

As provided above, the claims, as amended, recite both structural and functional properties of the claimed nucleic acid sequence. Thus, the claims do not provide that any sequence 80% identical to the listed sequence encodes a polypeptide having Helios biological activity. Instead, the claims require that the nucleic acid be at least 80% identical or be able to hybridize under stringent conditions to the listed sequences and that it encode a polypeptide having a Helios biological activity. Applicants have provided three species which meet the limitations of these claims. These are: a sequence encoding a murine Helios polypeptide (SEQ ID NO:1), a sequence encoding an isoform of murine Helios (SEQ ID NO:3), and a sequence encoding a human Helios polypeptide (SEQ ID NO:5). Thus, Applicants have clearly provided a sufficient number of species to demonstrate that Applicants were in possession of the claimed invention at the time of filing.

Therefore, Applicants respectfully request that the Examiner withdraw this rejection.

Claims 1-5, 10, 11 and 13 are also rejected under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." In particular, the Examiner states that

> [t]he specification provides adequate guidance for making SEQ ID NO:1, 3 and 5 and the use of these to make the encoded protein, and provides adequate teaching on how to make and use other nucleic acid sequences which encode a protein with similar sequence, however, the specification fails to provide guidance on use of the nucleic acid sequences. Further, as discussed above in the written description rejection, no guidance is given for making or using the nucleic acid sequences which meet the hybridization limitations, or react with an antibody, or fragment thereof.

Applicants respectfully traverse this rejection. As discussed above, the claims 1 and 3, as amended, are directed to nucleic acids which have at least 80% identity or have the ability to hybridize under high stringency conditions to the listed sequences, and which encode a polypeptide having a Helios biological activity. Claims 2, 10, 11 and 13 depend either directly or indirectly from these claims.

The Examiner admits that there is sufficient guidance in the present application to make both a sequence having the listed nucleotide sequences or a sequence encoding a protein with a similar amino acid sequence. The Examiner also admits that the present application provides a use for the nucleic acid sequences having the listed sequence to make the encoded protein. Since the claims, as amended, require that the nucleic acids, which encode a polypeptide with a similar amino acid sequence, also encode a polypeptide having a Helios biological activity, it is clear that the present application also provides sufficient guidance for use of these nucleic acids for making the encoded polypeptide.

The Examiner further asserts that

> [i]n the instant case there are a large number of nucleic acid sequences which contain 'at least about 60 amino acids' and share enough homology to hybridize to the recited SEQ ID Nos, however, these sequences encode various unrelated proteins. Therefore, while the specification provides the necessary guidance for one skilled in the art to make the polynucleotides Set forth in SEQ ID NO:1, 3 or 5, it does not provide the necessary guidance for one of skill in the art to use the

> nucleic acid sequences which do not encode a Helios protein. Further, since no functional language is associated with the Helios protein encoded by SEQ ID NO: 1, 3 or 5, one of ordinary skill in the art would not know how to use these defined sequences except in further characterization of the sequences themselves.

Claim 5, as amended, is directed to nucleic acid which encodes a fragment of the listed polypeptide sequence that is at least 60 amino acids in length. The nucleic acid hybridizes under high stringency conditions to a nucleotide encoding Helios but does not cross react with sequence encoding Ikaros or Aiolos. Applicants assert that such nucleic acids clearly have a use—they can be used to distinguish Helios from other proteins involved in hematopoiesis.

For the reasons discussed above, Applicants respectfully request that the Examiner withdraw this rejection.

Rejection of Claims 1-5, 10 and 11 Under 35 U.S.C. §112, second paragraph

Claims 1-5, 10 and 11 have been rejected under 35 U.S.C. §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention." Specifically, the Examiner asserts that

> Claim 1 is vague and unclear in the recitation of 'which is 60% identical to SEQ ID NO:1, 3 or 5' because the metes and bounds of identical are not clearly defined. It is unclear if the identity is over the full length of the sequence or if a sequence which is truncated by 40% of its sequence or deleted of 40% of its internal sequence would still be considered 60% identical. When read in light of the specification identity is the equivalent to homology (page 31; lines 4-14), though an example is provided, it is not clear if this example excludes deletions and truncations encompassed by the claims as written.

Applicants respectfully traverse this rejection. Claim 1, as amended, recites a nucleic acid which is at least 80% identical to SEQ ID NO:1, 3 or 5, and which encodes a polypeptide having a Helios biological activity. As provided at page 31, lines 14-17 of the present application, the sequences can be aligned for optimal comparison purposes (e.g., gaps can be introduced in first nucleic acid sequence for optimal alignment with the second nucleic acid sequence). It is clear, therefore, that the nucleic acid must have at least 80% sequence identity with the listed sequence. Where the sequence differences occur is not recited in the claim.

Therefore, that as long as the polypeptide encoded by the nucleic acid has a Helios biological activity, the differences in the nucleotide sequence of the listed sequences and the claimed sequence can include truncations and deletions.

The Examiner also rejected claim 3 as being "vague and indefinite in the recitation of 'under high stringency conditions' because the conditions are not specifically described in the specification or the claim, so the metes and bounds have not been adequately defined."

Applicants respectfully traverse this rejection. Page 56, line 28 of the present application provides that "for the definitions of high and low stringency conditions see Current Protocols in Molecular Biology." Applicants have since incorporated into the present application those sections of the Current Protocols in Molecular Biology which set forth two wash conditions considered to be high stringency conditions. In view of this information, it is clear that the high stringency conditions referred to in claim 3 refer to nucleic acid sequences which hybridize under those conditions specified as high stringency in the added section.

For the reasons discussed above, Applicants respectfully request that the Examiner withdraw this rejection.

Conclusion

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be allowed. Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 7/5/01

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Version with markings to show changes made

In the claims:

Claims 4, 15 and 16 have been cancelled.

Claims 1-3, 5, 10 and 11 have been amended as follows

--1. (Amended) A substantially pure nucleic acid comprising a nucleotide sequence which is at least [60%] 80% identical to the nucleotide sequence of SEQ ID NO:1, 3 or 5, and which encodes a polypeptide having a Helios biological activity.

2. (Amended) The nucleic acid of claim 1, comprising the nucleotide sequence of SEQ ID NO:1, 3, or 5.

3. (Amended) [The] A substantially pure nucleic acid [of claim 1, wherein the nucleic acid] which hybridizes under high stringency conditions to the nucleotide sequence of SEQ ID NO:1, 3, or 5, and which encodes a polypeptide having a Helios biological activity.

5. (Amended) A substantially pure nucleic acid which encodes a fragment of the polypeptide of SEQ ID NO:2, 4, or 6 of at least 60 amino acids in length and which hybridizes under high stringency conditions to a nucleotide of SEQ ID NO:1, 3 or 5, wherein the nucleic acid does not cross react with an Ikaros gene or an Aiolos gene.

10. (Amended) A vector comprising the nucleic acid of any of claims 1, 2, or 3[, 4, or 5].

11. (Amended) A cell comprising the nucleic acid of any of claims 1, 2, or 3[, 4, or 5].